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RESEARCH ARTICLE

Scalp block for awake craniotomy: Lidocaine-bupivacaine versus lidocaine-bupivacaine with adjuvants

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ABSTRACT

Methodology: Forty patients were randomly allocated into 4 equal groups based on LA mixture used for scalp block: **Group I**:received 1.5 mg/kg bupivacaine 0.25% + 5 mg/kg lidocaine 1% with 1:200,000 epinephrine. **Group II**:same as Group I + 8 mg dexamethasone. **Group III**:same as Group I + 500 mg$MgSO_4$. **Group IV**:same as Group I + 8 mgdexamethasone + 500 mg$MgSO_4$. Dexmedetomidine was used for intraoperative sedation and paracetamol for postoperative analgesia.

Results: Total intra-operative consumption of dexmedetomidine was highly significantly less in Group II (232 ± 21 µg) and Group III (241 ± 18 µg) compared to Group I (286 ± 27 µg). Group IV (162 ± 25 µg) was highly significantly less than other groups. Time to first paracetamol requirement was highly significantly longer in Group II (245 ± 32 min) and Group III (236 ± 28 min) compared to Group I (187 ± 17 min). Group IV (388 ± 14 min) showed a highly significant longer time than other groups. Group IV consumed highly significant less doses of paracetamol in the first postoperative day (POD1) (2.2 ± 0.1 g) than Group I (2.9 ± 0.4 g), Group II (2.7 ± 0.3 g) and Group III (2.8 ± 0.5 g).Pain in POD1 was significantly higher in Group I at after 3 h of surgery compared to other groups. VAS was comparable during the rest of the times of the study among the four groups. All patients were hemodynamically stable during times of the study. Blood glucose levels were within normal levels with no significant differences between the groups within 6 hof scalp block.

Conclusion: Adding either 8 mg©dexamethasone or 500 mg©MgSO4 or both to bupivacaine-lidocaine for scalp block before awake craniotomy improves performance of the block with the best results when combined.

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Awake craniotomy; scalp block; dexamethasone; magnesium sulfate

1. Introduction

Awake craniotomy using cortical and/or subcortical brain mapping enables better resection of brain tumors with decreased possibility of functional damage to the patient [1,2].

Awake craniotomy can be defined as a sort of craniotomy in which the patient is conscious and responsive at any time during the procedure [3]. It might be performed under one of three different forms of anesthetic care. Sleep–awake–sleep technique is based upon anesthetizing the patient during skull-pin head holder, and then consciousness must be regained during brain mapping of cortical areas. Another technique might be performing monitored anesthetic care with the patient mildly sedated all through the procedure. Lastly, the awake all-through technique in which no sedation is provided. It only requires analgesia and special attention to non-pharmacological interventions such as hypnosis [4]. Local anesthesia is the cornerstone in awake craniotomy surgeries [5–7]. In awake all-through technique, effective local anesthetics is mandatory [3].

A large volume of local anesthetic (up to 60 mL) in the well-vascularized scalp might hit the margin of anesthetic toxicity easily [8]. Adding adrenaline (5 µg/mL, 1:200 000 dilution) prevents the acute rise in plasma concentration and prolongs the duration of the block [9,10]. Bupivacaine is the most commonly used local anesthetic for scalp block [11], while ropivacaine and levobupivacaine might also be used [6,12,13]. Mixing two local anesthetics (e.g. lidocaine and bupivacaine) is an old idea that has been used to gain rapid onset and long-duration analgesia and helps avoiding toxic doses of both drugs [14].

Dexamethasone has been found to prolong the duration of action of local anesthetics providing better analgesic efficacy in both regional anesthesia and peripheral nerve blocks [15–17]. However, other studies found that there was no statistically significant prolongation of local anesthesia when dexamethasone was added [18,19].

N-methyl D-aspartate (NMDA) receptors are ionic-glutamate receptors in nerve cells that play an important role in pain process [20]. Magnesium blocks NMDA receptors [21] and blocks calcium channels thus potentiating opioid-induced analgesia [22].

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The aim of the current study was to detect the safest and most effective adjuvant(s) to be added to local anesthetic mixture used for scalp block during awake craniotomy. It was hypothesized that adding either dexamethasone, magnesium sulfate, or both to lidocaine-bupivacaine during scalp block might decrease the consumption of sedatives used during procedural sedation in awake craniotomy. It was also hypothesized that it might provide better postoperative analgesia.

2. Patients and methods

This randomized, prospective double-blinded controlled study was conducted in Zagazig University Hospitals after obtaining institutional ethics committee approval. Written informed consent was obtained from all patients. The study was performed between January 2016 and September 2018, on 40 patients who were posted for awake craniotomy surgeries due to intracranial mass near eloquent areas in the dominant hemisphere. Patients enrolled in the study aged between 21 and 60 years of both sexes, with body mass index (BMI) of 18.5–29.9 kg/m^2, belonging to ASA physical status of II or III. Exclusion criteria included: refusal of the patient, pregnancy, bleeding disorders or patients on anticoagulants, presence of cardiac or respiratory disease, diabetics, local infection at site of injection, patients with known allergy to any of the study drugs, patients receiving sedatives, psychological disturbances, alcohol or substance abuse, and those who did not fulfill inclusion criteria.

Patients selected for the procedure of awake craniotomy had to pass psychological tests. Multiple visits to the patient to get patient confidence and trust, and to perform a thorough explanation of the procedure were done.

2.1. Randomization and allocation

Patients were randomly allocated into four groups using closed envelop method. Allocation was based upon the adjuvant(s) added to local anesthetic (LA) mixture used for scalp block into:

Group I (n = 10): received LA mixture of: 1.5 mg/kg bupivacaine (0.25%) + 5 mg/kg lidocaine (1%) with 1:200,000 epinephrine.

Group II (n = 10): received LA mixture of: 1.5 mg/kg bupivacaine (0.25%) + 5 mg/kg lidocaine (1%) with 1:200,000 epinephrine + 8 mg (2 mL) dexamethasone.

Group III (n = 10): received LA mixture of: 1.5 mg/kg bupivacaine (0.25%) + 5 mg/kg lidocaine (1%) with 1:200,000 epinephrine + 500-mg magnesium sulfate (5 mL of 10% magnesium sulfate).

Group IV (n = 10): received LA mixture of: 1.5 mg/kg bupivacaine (0.25%) + 5 mg/kg lidocaine (1%) with 1:200,000 epinephrine + 8 mg (2 mL) dexamethasone + 500 mg magnesium sulfate (5 mL of 10% magnesium sulfate).

For all patients, the total volume of LA ranged between 60 and 90 mL which was used for circumferential scalp block, field block, as well as local anesthesia at sites of pin insertion.

2.2. Anesthetic plan and scalp block

None of the patients were sedated during premedication. Therapeutic serum levels of the anticonvulsant therapy were achieved days before surgery. On the day of surgery, the morning dose of phenytoin was doubled from 5 to 10 mg/kg, then resumed on 5 mg/kg after surgery. At operation room (OR)3 L/min oxygen was delivered through nasal cannula. Intravenous 8 mg Ondansetron, 8 mg dexamethasone and prophylactic antibiotics were given. Routine monitoring was applied including electrocardiogram (ECG), noninvasive blood pressure monitoring, oxygen saturation (SPO_2), respiratory rate and end-tidal carbon dioxide ($ETCO_2$) measured via an $ETCO_2$ nasal cannula.

All patients were placed in a comfortable position suitable for surgery. Before circumferential scalp block, all patients were given IV propofol (1 mg/kg) and fentanyl (1 μ/kg).

The higher dose limits of LA were calculated individually for each patient as 2–3 mg/kg for bupivacaine, 5 mg/kg for lidocaine, and 7 mg/kg for lidocaine plus epinephrine.

Circumferential scalp block was performed using 3-5 mL of LA for each of the branches responsible for sensory supply of the forehead and scalp including supraorbital, supratrochlear, zygomaticotemporal, auriculotemporal, greater occipital, and lesser occipital nerves (Figure 1) as follows:

1- Supraorbital and Supratrochlear nerves: LA was injected 1 cm medial to supraorbital foramen to block the supraorbital nerve. Then, 1 cm medially to block the supratrochlear nerve.

2- Zygomaticotemporal nerve: LA was injected just above the zygoma at the posterior portion of the zygomatic arch.

3- Auriculotemporal nerve: LA was injected at the level of the zygoma, about 1 cm anterior to the tragus (superficial temporal artery was palpated to avoid intraarterial injection).

4- Greater occipital nerve: LA was injected at the midpoint between the occipital protuberance and the mastoid process (about 2.5 cm lateral to the occipital protuberance). The occipital artery was palpated to avoid intraarterial injection.

5- Lesser occipital nerve: LA was injected along the superior nuchal line, about 2.5 cm lateral to the point of injection for the greater occipital nerve block, or roughly 5 cm lateral to the occipital protuberance.

Field block at site of incision was done using 15–20 mL of LA. Last, the sites of pin insertion were

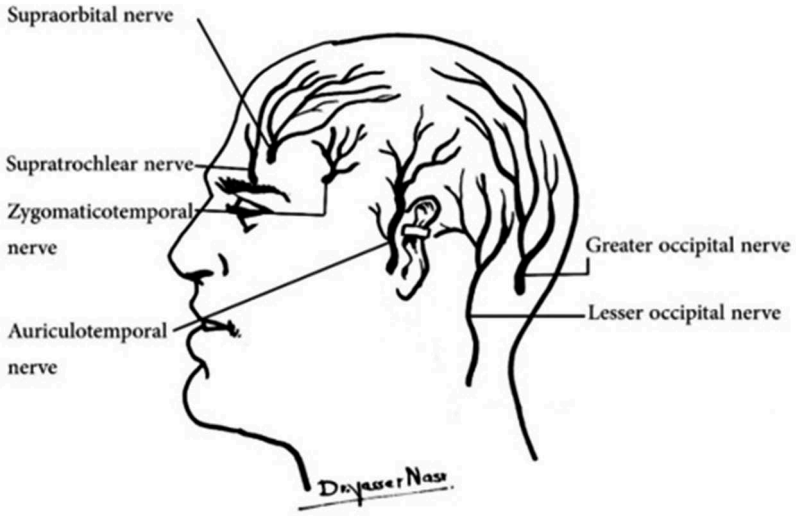

Figure 1. A drawing for the main branches responsible for the cutaneous sensory innervations of the forehead and scalp.

also infiltrated using 2 cm lidocaine 2% with 1:200,000 epinephrine.

2.3. For all patients

- Asleep Awake-throughout technique was applied for all patients. The targeted level of sedation was a Ramsay Sedation Scale [23] (RSS) of 2–3 during the time of cortical mapping, while before and after that the patient was maintained at RSS of 5–6.

  - Patients received propofol infusion at a rate of 25–75 µ/kg/min which was stopped approximately 15–20 min before starting cortical mapping and was resumed again during wound closure.
  - Fentanyl was given 25µ bolus every 30 min on regular pattern.
  - An initial loading dose of 1 µg/kg dexmedetomidine was given intravenously over 20 min, followed by continuous infusion of 0.1–0.7 µg/kg/h as a maintenance dose using a syringe pump. The dose of dexmedetomidine was reduced to 0.1 µg/kg/h 15–20 min before starting cortical mapping. Higher levels of maintenance dose were resumed during wound closure according to patient's need.
  - Emergency airway management strategies were pre-prepared if to be needed including: the availability and readiness of laryngeal mask airway (LMA), endotracheal tube (ETT), laryngoscope, fiber-optic endoscope, as well as tracheostomy kit. General anesthesia measures were also available and ready to be performed at any time.
- Urinary catheter was not applied as it causes patient discomfort [24]. Urinary convene was prepared to be used if needed (e.g. if diuretics were used or if duration of surgery exceeded 4 h). Judicious use of fluids was considered and IV fluids were supplied as normal saline (50–100 ml/h).
- Ice-cold saline was always pre-prepared for cortical irrigation in case of occurrence of intraoperative stimulation-induced seizures. Propofol (0.5 mg/kg) was planned to be used to control seizures if occurred.
- All Patients were transferred to post-anesthetic care unit (PACU) when Ramsay sedation score [24] (RSS) = 2 (Table 1). They stayed in PACU for 4–8 h before being transferred to the neurosurgery ward.
- Postoperative analgesia was planned as IV paracetamol. The first dose was given according to the patient's need using a visual analog scale [25] (VAS) ≥4which was considered as inadequate pain relief (0 = no pain, and 10 = worst pain possible).Then, 1 g IV paracetamol/8 h was maintained for the first 48 h of postoperative period (with a minimum gap of 6 h and a maximum dose of 4 gm/day of IV paracetamol according to patient's need).

2.4. Collected data

In addition to patient characteristics, the following data were also recorded by a physician who was blinded to the protocol of the study:

(1) Duration of surgery starting from skin incision to skin closure.
(2) Degree of pain according to VASevery 1 h during the intraoperative period. VAS was then recorded during the first day of

Table 1. Ramsay sedation scale [23].

Score	Response
1	Anxious or restless or both
2	Cooperative, oriented and tranquil (calm)
3	Responding to command
4	Brisk (quick) response to stimulus
5	Sluggish (slow moving) response to stimulus
6	No response to stimulus

postoperative period (POD1) at the following times: 0, 3, 6, 12, 24 where T_0 = time of arrival of the patient to PACU.

(3) Total intra-operative consumption of dexmedetomidine and propofol.
(4) Time to first dose of postoperative analgesia with IV paracetamol when VAS was ≥4.
(5) Total consumption of paracetamol in POD1.
(6) Cases of intraoperative over-sedation if occurred (over-sedation were defined as the patient needing >20 min to reach RSS of 3 to be able to respond to commands after stopping all sedative infusions during cortical mapping).
(7) Duration of recovery from sedation by the end of surgery: defined as time from stopping all infusions until the time to be ready to transfer to PACU when RSS = 2.
(8) Blood glucose level was measured every 1 h during intraoperative periods.
(9) Mean arterial blood pressure (MAP), heart rate (HR), respiratory rate (RR), and oxygen saturation (SPO_2) were recorded. The following definitions were considered:
   - Hypertension (MAP ≥ 30% of basal readings (recorded the day before surgery) on two consecutive readings and managed according to the cause whether pain, anxiety, hypothermia, or hypoxia).
   - Hypotension (MAP ≤ 30% of basal, managed by IV fluids and vasopressors if needed).
   - Tachycardia (HR≥110 b/min and managed according to the cause whether pain, anxiety, hypothermia or hypoxia).
   - Bradycardia (HR ≤ 60 b/min, managed with 0.1 mg/kg atropine sulfate and check the cause),
   - Bradypnea (RR < 12 breath/min, managed by lowering or stopping the hypnotic and/sedative) and applying non-invasive continuous positive airway pressure (CPAP) if needed).
   - Hypoxia (SPO_2 < 92% on nasal cannula 3 L/min, managed by maintaining airway and applying non-invasive CPAP).
(10) Postoperative complications such as nausea, seizures, airway obstruction, or respiratory depression were recorded if occurred.

2.5. Sample size

The sample size was calculated after conducting a pilot study (5 patients in each group) to detect a significant difference in intraoperative consumption of dexmedetomidine during awake craniotomy. G*POWER program [version 3.1.9.2 (Heinrich Heine; Universitat Dusseldorf; Germany)] was used prospectively to calculate the power of this study. It was calculated that a sample size of 10 per group was required to give $P < 0.5$ significance with a confidence interval 95% with a power of 80%.

2.6. Statistical analysis

The software Statistical Package for the Social Sciences (SPSS version 20.0) was used to analyze the data obtained from the current study. Qualitative data were represented as number and percentage. Quantitative data were represented by mean ± SD or median and range. The following tests were used when appropriate: Chi-square test (X^2), ANOVA or Kruskal Wallis. P value was set at <0.05 for significant results and <0.001 for highly significant results.

3. Results

In the current study, 40 patients were enrolled in the study, and none of them were excluded from statistical analysis as shown in the flow chart (Figure 2).

Patients' characteristics and data of surgeries showed no statistical differences between the four groups as shown in (Table 2). None of the patients was recorded as over-sedated and duration of recovery from sedation by the end of surgery was comparable between the four groups (Table 2).

Total intra-operative consumption of propofol showed no statistical differences among the four groups (Table 3). Total intra-operative consumption of dexmedetomidine (Table 3) showed statistically high significant less doses in Group II (232 ± 21 µg) and Group III (241 ± 18 µg) compared to Group I (286 ± 27 µg). Group IV (162 ± 25 µg) showed statistically high significant less doses than the other three groups. Time to first paracetamol requirement (Table 3) was statistically highly significant longer in Group II (245 ± 32 min) and Group III (236 ± 28 min) compared to Group I (187 ± 17 min). Group IV (388 ± 14 min) showed a statistically highly significant longer time than the other three groups. Regarding the total consumption of paracetamol in the first postoperative day,

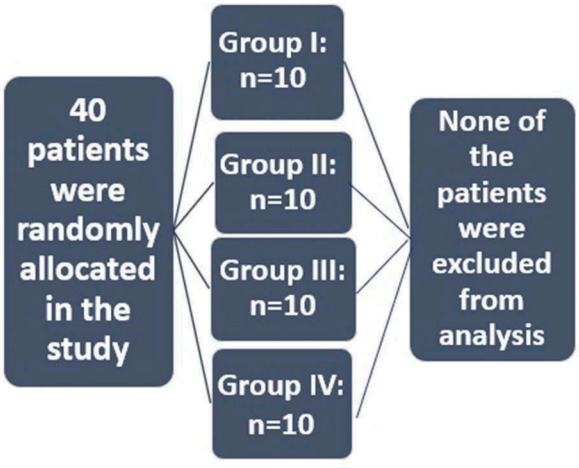

Figure 2. Flow chart of the study.

Table 2. Patients' characteristics and surgical data.

Variable	Group I (n = 10)	Group II (n = 10)	Group III (n = 10)	Group IV (n = 10)	P value
Age (y)	**33 (22–48)**	**34 (30–47)**	**31 (23–44)**	**34 (25–47)**	**0.643**
BMI (kg/m^2)	**27.6 ± 1.2**	**27.1 ± 1.4**	**28.3 ± 1.5**	**28.1 ± 1.1**	**0.187**
Sex: Male/Female (*n*)	**6/4**	**7/3**	**5/5**	**8/2**	**0.523**
ASA II/III (*n*)	**9/1**	**7/3**	**6/4**	**8/2**	**0.446**
Surgical data					
• Side of the tumor (right/left)	**4/6**	**5/5**	**3/7**	**4/6**	**0.841**
• Duration of surgery (min)	**207.1 ± 15**	**203.8 ± 19**	**206.5 ± 16**	**208.2 ± 11**	**0.932**
• Duration of recovery from sedation by the end of surgery (min)	**22.5 ± 0.7**	**21.1 ± 1.1**	**20.3 ± 0.8**	**21.6 ± 0.9**	**0.955**

p value was considered statistically significant when <0.05. Data are represented as median (range), mean ± SD, or number.
BMI: body mass index. ASA: American Society of Anesthesiologists.

Table 3. Analgesic performance in the four groups of the study.

Variable	Group I (n = 10)	Group II (n = 10)	Group III (n = 10)	Group IV (n = 10)	P value
Total intraoperative consumption of propofol/patient (mg)	104 ± 18	100 ± 13	98 ± 16	94 ± 10	0.493
Total intraoperative consumption of dexmedetomidine/patient (μg)	286 ± 27	232 ± 21**	241 ± 18**	162 ± 25§§	<0.001
Time to first paracetamol requirement (min): VAS ≥4	187 ± 17	245 ± 32**	236 ± 28**	388 ± 14§§	<0.001
Total consumption of paracetamol in POD1/patient (g)	2.9 ± 0.4	2.7 ± 0.3	2.8 ± 0.5	2.2 ± 0.1§§	<0.001

p value was considered statistically significant when <0.05 and highly statistically significant when <0.001.
Data are represented as mean ±SD.
** Highly statistically significant difference when compared to Group I.
§§ Highly statistically significant difference when compared to the other three groups.
VAS: visual analog scale.

Group IV (2.2 ± 0.1 g) showed statistically high significant less doses than Group I (2.9 ± 0.4 g), Group II (2.7 ± 0.3 g) and Group III (2.8 ± 0.5 g) (Table 3).

Intraoperative pain scores according to VAS were comparable between the four groups and ranged between 0 and 1. Figure 3 shows pain during the first postoperative day (according to VAS) was comparable at T_0. However, statistically significantly higher scores were recorded in Group I at T_3 compared to the other groups. During the rest of the times of the study, there were no statistically significant differences among the four groups in regards to VAS.

Regarding hemodynamics, none of the patients in this study has experienced intraoperative hypertension or hypotension and readings were comparable between groups (Figure 4). Heart rate, respiratory rate, and oxygen saturation were also comparable between groups with no recorded intraoperative complications.

Blood glucose levels were within normal levels and showed no statistically significant differences between the four groups of the study within 6 hours of scalp block (Table 4).

There were no postoperative complications during the first postoperative day such as nausea, seizures, airway obstruction, or respiratory depression.

4. Discussion

The results obtained in the current study showed that adding either dexamethasone or magnesium sulfate or both to lidocaine-bupivacaine used for local anesthetic block of the scalp during awake craniotomy resulted in better performance of the block during both intraoperative or postoperative periods. To our knowledge, no previous researches have studied the effect of adding these adjuvants to local anesthesia for scalp block during awake craniotomy.

Scalp infiltration with local anesthetic has been studied as a method to decrease postoperative pain [26]. In their study, Osborn and Sebeo [26] mentioned that in the early years of the last century, Harvey Cushing and George Crile performed their studies to combine local anesthetic infiltration with general anesthesia in craniotomies. Moreover, subcutaneous infiltration of local anesthetics mixed with vasopressors has been used since the early 1900s [26]. Thereafter, this mixture has been injected and widely used before scalp incision to help hemostasis [27,28].

Hillman et al. [29] performed the first double-blind randomized study comparing the effects of local infiltration of the scalp using 0.5% bupivacaine to normal saline injection in patients undergoing craniotomies and concluded better cardiovascular hemodynamic stability with bupivacaine. Bupivacaine became the local anesthetic of choice for local infiltration of the scalp due to its reported safety and long duration of action [30,31]. Moreover, Bithal et al. [32] showed that local anesthetic infiltration at sites of skull pinning was accompanied by lower bispectral index and hemodynamic stability.

This pathway led eventually from scalp infiltration to scalp block which was first described for awake craniotomy by Girvin [33] in 1986. Multiple studies have been performed later on and supported the use of bupivacaine for scalp block [34,35].

In the current study, there were no intraoperative increase in blood pressure or heart rate which comes in agreement with the results obtained by previous

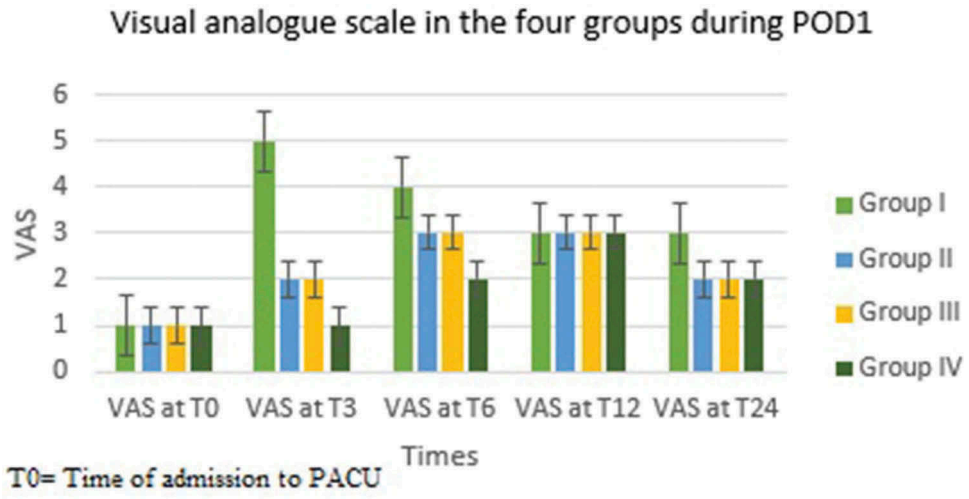

Figure 3. Degree of pain during the first postoperative day (POD1) according to visual analog scale [25] (VAS) in the four groups of the study. Data were presented by median and range.

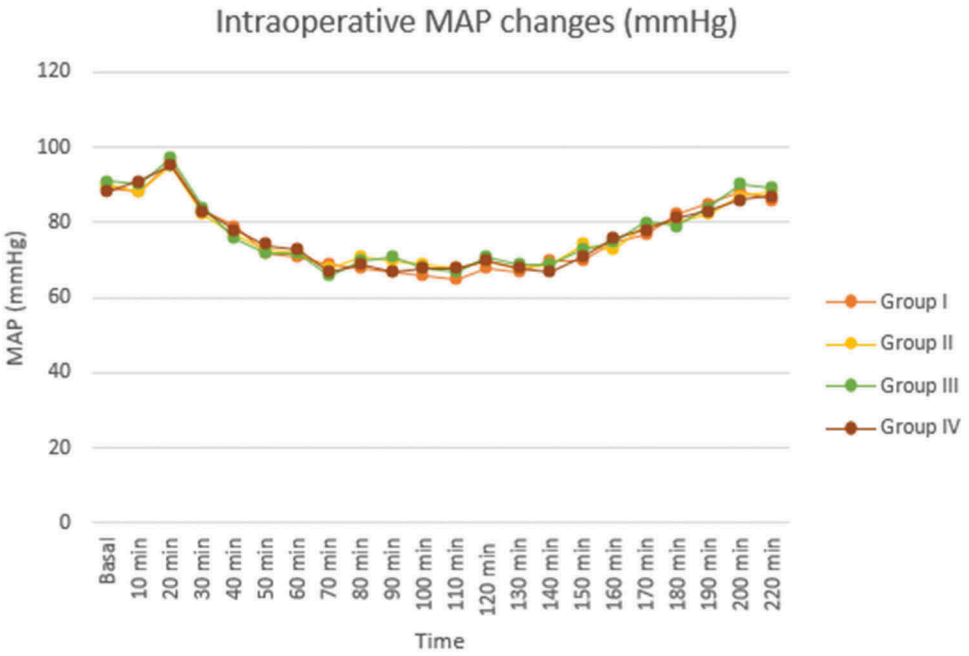

Figure 4. Intraoperative changes in MAP (mmHg) in the four groups of the study.

Table 4. Blood glucose level (mg/dL) in the four groups of the study.

Variable	Group I (n = 10)	Group II (n = 10)	Group III (n = 10)	Group IV (n = 10)	P value
Just before scalp block	95.1 ± 4.2	97.3 ± 3.3	98.9 ± 5.7	96.1 ± 5.1	0.313
2 h after scalp block	93.3 ± 6.1	95.4 ± 5.2	97.7 ± 3.9	96.8 ± 4.1	0.224
4 h after scalp block	98.1 ± 2.2	96.6 ± 5.3	97.1 ± 4.3	95.1 ± 4.7	0.476
6 h after scalp block	95.8 ± 3.9	94.9 ± 3.7	96.2 ± 4.6	94.5 ± 5.2	0.811

p value was considered statistically significant when <0.05 and highly statistically significant when <0.001.
Data are represented as mean ±SD.

studies that stated that during surgery, local anesthesia reduces the hemodynamic responses occurring during the application of Mayfield clamp [5,36]and during closure of the dura and the skin [37]. The brain tissue itself lacks sensory innervation, thereby, these times of surgery are much more painful than tumor resection [38].

Pain after craniotomy was reported to be moderate or severe particularly in the first 2 h after craniotomy [39]. Postoperative pain control in neurosurgery should keep the balance between providing the best conditions for neurological assessment (e.g. preventing sedation) on one side and providing patient comfort on the other side [3]. The use of a local anesthetic scalp block was

found to provide postoperative pain control following craniotomyin in the early postoperative period [40,41], which comes in accordance with the results obtained in the present study. Moreover, the use of adjuvants in this study significantly increased the postoperative pain-free duration and reduced the postoperative consumption of paracetamol in the first postoperative day.

Dexamethasone has been found to improve the postoperative performance of pain when used as an adjuvant to bupivacaine [17,42,43]. This might be explained by induced vasoconstriction with reduced absorption of local anesthetic, or by potentiation of inhibitory potassium channels on nociceptive c-fibers resulting in prolonged nerve block [44].In this study, none of the patients were diabetic and none of those who were given dexamethasone developed hyperglycemia. However, adding a glucocorticoidto local anesthetics may not be appropriate for every patient as diabetics might experience hyperglycemia as a single perioperative dose of dexamethasone has been found to elevate intraoperative blood glucose for almost 4 h in a study by Zhang et al. [45]. To date, dexamethasone-induced neuronal damage has not been reported. Moreover, in vitro animal studies found that dexamethasone attenuatedbupivacaine-induced neurotoxicity which might result in transient neurological syndrome (TNS) [46].

Physical compatibility and chemical stability of magnesium sulfate and lidocaine mixtures were previously studied when combined and were found to be stable with no changes in pH, color, or precipitates and can even be manufactured in a pre-filled (Magnocaine) syringe duration of stability of at least 6 months in high heat and humidity conditions [47].

Scalp block is a safe technique with rare complications reported in literature [26]. In spite of being rare, complications have been reported with scalp blocks mostly due to inadvertent injection of the local anesthetic into circulation [48]. Thereby, close monitoring should be performed during the first 15 min of injection of local anesthetics for awake craniotomies [9,10,12].Archer et al. [49] was the only study to report local anesthetic toxicity during awake craniotomy with questionable results since their study was conducted upon 354 epileptic patients with intractable seizures undergoing awake craniotomy. Only 2% of these patients developed temporary convulsions, and the authors related them to local anesthetic toxicity. In the current study, there were no complications recorded in association with scalp block.

5. Limitation of the study

The study was not extended to evaluate whether the incidence of post-craniotomy pain was affected by these mixtures or not.

6. Conclusion

Adding either dexamethasone (8 mg) or magnesium sulfate (500 mg) or both to bupivacaine 0.25% and lidocaine 1% with 1:200,000 epinephrine, for scalp block before awake craniotomy was associated with better performance of the block during both intraoperative or postoperative periods. Adding both dexamethasone and magnesium sulfate together was the best combination since it resulted in lower intraoperative consumption of sedatives as well as long-lasting postoperative pain relief.

Disclosure statement

No potential conflict of interest was reported by the authors.

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